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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/581,544	07/08/2008	Edward Daniel Savory	13425-193US1 BV-1088 US	3943
26161 7590 11/22/2010 FISH & RICHARDSON P.C. (BO) P.O. BOX 1022 MINNEAPOLIS, MN 55440-1022			EXAMINER LAU, JONATHAN S	
			ART UNIT 1623	PAPER NUMBER
			NOTIFICATION DATE 11/22/2010	DELIVERY MODE ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

Office Action Summary	Application No. 10/581,544	Applicant(s) SAVORY, EDWARD DANIEL	
	Examiner Jonathan S. Lau	Art Unit 1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 September 2010.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-40 is/are pending in the application.
- 4a) Of the above claim(s) 34-36 and 38-40 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-33 and 37 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>3 pgs / 6 Nov 2006</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

This application is the national stage entry of PCT/GB04/005092, filed 3 Dec 2004; and claims benefit of foreign priority document UNITED KINGDOM 0328323.1, filed 5 Dec 2003; this foreign priority document is in English.

Claims 1-40 are pending in the current application. Claims 34-36 and 38-40, drawn to non-elected inventions, are withdrawn. Claims 1-33 and 37 are examined on the merits herein.

Election/Restrictions

Applicant's election without traverse of Group I, claims 1-33 and 37 in the reply filed on 30 Sep 2010 is acknowledged.

The requirement is still deemed proper and is therefore made FINAL.

Claims 34-36 and 38-40 withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 30 Sep 2010.

Applicant's election of species of spongosine in the reply filed on 30 Sep 2010 is acknowledged.

For the purpose of facilitating prosecution, this election of species requirement is **withdrawn**.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-10, 12-31 and 37 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the method of synthesis of a 2-substituted adenosine of formula I comprising converting a compound of formula II to a compound of formula I wherein R is an alkoxy, phenoxy or benzyloxy group, does not reasonably provide enablement for said method wherein R is a benzoyl group. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The Applicant's attention is drawn to *In re Wands*, 8 USPQ2d 1400 (CAFC1988) at 1404 where the court set forth eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) The nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the

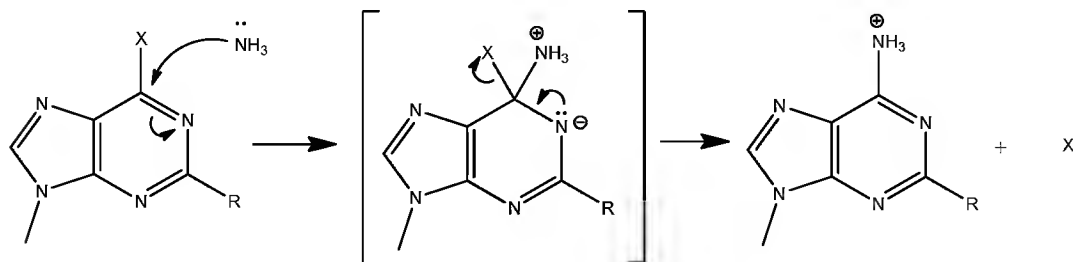
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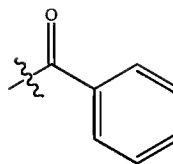
claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

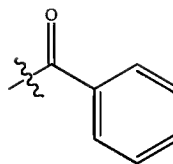
Nature of the invention: A method of synthesis of a 2-substituted adenosine of formula I comprising converting a compound of formula II to a compound of formula I.

The state of the prior art: Schaeffer et al. (JACS, 1958, 82, p3738-3742, provided by Applicant in IDS mailed 6 Nov 2006) teaches nucleophilic aromatic substitution (page 3738, left column paragraph 2) of a dichloropurine with methanolic ammonia to displace a chloride (page 3739, chart I at top of left column and right column, paragraph 4). Schaeffer et al. teaches conversion of the 6-amino-2-chloropurine to 6-amino-2-methoxypurine (page 3740, left column, chart III and paragraph 2).

Streitwieser et al. (Introduction to Organic Chemistry, 1992, 4th ed., p1006-1009, cited in PTO-892) teaches the ordinary level of skill in the art with regard to nucleophilic aromatic substitution. Streitwieser et al. teaches the leaving group X of the nucleophilic aromatic substitution leaves with a negative charge (top of page 1008). For example, when ammonia acts as a nucleophile to displace a leaving group from an aromatic system, the ammonium group retains a positive charge and the leaving group leaves with a negative charge:





It is well-known in the art that a benzoyl group, , does not easily act as a leaving group in nucleophilic substitution reactions because the resulting carbanion is a high energy species.

The relative skill of those in the art: The relative skill of those in the art is high.

The predictability or unpredictability of the art: While the reactivity of most chemical functionalities is relatively predictable, the sheer number of possible reactions involving any possible reagents or reaction conditions means that one skilled in the art cannot predict the usefulness for all possible methods of synthesis. Therefore the claimed invention is unpredictable.

The Breadth of the claims: The scope of the claims is infinite. Any possible reagents or reaction conditions could potentially be used as the method of synthesis. Claims 1 and 2 recite the method wherein R is selected from the group including a benzoyl group.

The amount of direction or guidance presented: The specification speaks generally about a nucleophilic aromatic substitution, such as use of ammonia to convert a compound of formula II to a compound of formula I at page 5, paragraph 1. However, guidance is not given for reagents other than ammonia, or a nucleophilic aromatic substitution reaction.

The presence or absence of working examples: The only working examples provided are for reaction wherein R is a C₁ alkoxy group and the conversion of a

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compound of formula II to a compound of formula I is performed using ammonia (page 14, step 5 in scheme 1).

No working examples are provided wherein R is a benzoyl group.

Note that lack of working examples is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art such as all possible organic synthesis. See MPEP 2164.

The quantity of experimentation necessary: In order to practice the invention with the full range of all possible reactions beyond those known in the art, (such as the method wherein R is an alkoxy, phenoxy or benzyloxy group) one skilled in the art would undertake a novel and extensive research program into the full scope of organic synthesis. Because this research would have to be exhaustive, and because it would involve such a wide and unpredictable scope of reagents and reaction conditions, it would constitute an undue and unpredictable experimental burden.

Genentech, 108 F.3d at 1366, states that, "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion." And "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

Therefore, in view of the Wands factors, as discussed above, particularly the breadth of the claims, Applicants fail to provide information sufficient to practice the claimed invention of said method wherein R is a benzoyl group.

Claim 10 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the method of synthesis of a compound of formula II comprising converting a compound of formula II to a compound of formula III

to a compound of formula I wherein R is an alkoxy, phenoxy or benzyloxy group, does not reasonably provide enablement for said method wherein R is a benzoyl group or wherein R is undefined. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

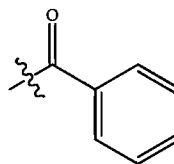
The Applicant's attention is drawn to *In re Wands*, 8 USPQ2d 1400 (CAFC1988) at 1404 where the court set forth eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

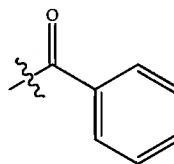
(1) The nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Nature of the invention: A method of synthesis of a 2-substituted adenosine of formula I comprising converting a compound of formula II to a compound of formula I.

The state of the prior art: Wanner et al. (Bioorganic and Medicinal Chemistry Letters, 2000, 10, p2141-2144, provided by Applicant in IDS mailed 6 Nov 2006) teaches nucleophilic substitution of a 6-amino-2-nitropurine with MeOH in the presence of a weak base KCN to displace the nitro group (page 2142, scheme 1 at top of left column). One of ordinary skill in the art understands that MeOH in the presence of a weak base acts as a nucleophile and the nitro group acts as a leaving group.

Streitwieser et al. (Introduction to Organic Chemistry, 1992, 4th ed., p1006-1009, cited in PTO-892) teaches the ordinary level of skill in the art with regard to nucleophilic aromatic substitution. Streitwieser et al. teaches the leaving group X of the nucleophilic aromatic substitution leaves with a negative charge (top of page 1008).



It is well-known in the art that a benzoyl group, , does not act as a nucleophile in nucleophilic substitution reactions because the carbonyl carbon has a partial positive charge.

It is well-known in the art that a benzoyl group may be added via electrophilic aromatic substitution by Friedel-Crafts acylation, however electrophilic aromatic substitution implies the loss of a positively charged leaving group, commonly H^+ .

The relative skill of those in the art: The relative skill of those in the art is high.

The predictability or unpredictability of the art: While the reactivity of most chemical functionalities is relatively predictable, the sheer number of possible reactions involving any possible reagents or reaction conditions means that one skilled in the art cannot predict the usefulness for all possible methods of synthesis. Therefore the claimed invention is unpredictable.

The Breadth of the claims: The scope of the claims is infinite. Any possible reagents or reaction conditions could potentially be used as the method of synthesis. Claim 1 recites the compound of formula II encompasses the compound wherein R is a benzoyl group. However, claim 10 does not depend from claim 1 and incorporate all limitations therein, and the formula II does not in itself define the groups R' or R.

The amount of direction or guidance presented: The specification speaks generally about the use of methoxide nucleophile to convert a compound of formula III to a compound of formula II at page 7, paragraph 1. However, guidance is not given for reagents other than an alkoxide for a nucleophilic aromatic substitution reaction.

The presence or absence of working examples: The only working examples provided are for reaction wherein R is a C₁ alkoxy group and the conversion of a compound of formula III to a compound of formula II is performed using sodium methoxide (page 14, step 4 in scheme 1).

No working examples are provided wherein R is a benzoyl group.

Note that lack of working examples is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art such as all possible organic synthesis. See MPEP 2164.

The quantity of experimentation necessary: In order to practice the invention with the full range of all possible reactions beyond those known in the art, (such as the method wherein R is an alkoxy, phenoxy or benzyloxy group) one skilled in the art would undertake a novel and extensive research program into the full scope of organic synthesis. Because this research would have to be exhaustive, and because it would involve such a wide and unpredictable scope of reagents and reaction conditions, it would constitute an undue and unpredictable experimental burden.

Genentech, 108 F.3d at 1366, states that, "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion." And "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

Therefore, in view of the Wands factors, as discussed above, particularly the breadth of the claims, Applicants fail to provide information sufficient to practice the claimed invention of said method wherein R is a benzoyl group or wherein R or R' are undefined.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3, 9-11, 14-33 and 37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3 recites "wherein R' is a protecting group that can be removed under conditions that replace the R group with an amino group at the 6-position of the purine component of the compound of formula II." This renders the claim indefinite because it is the conditions to replace the R group with an amino group at the 6-position will depend on the R group, and claim 3 does not require the R group to be a specific group. It is unclear what is required of the R' protecting group if the definition is dependent on the R group at the 6-position of the purine and that R group can be varied. Therefore one of ordinary skill in the art would not be readily apprised of the metes and bounds of the claim because it defines one variable with another variable.

Claim 10 recites "synthesis of a compound of formula II which comprises converting a compound of formula III to the compound of formula II". Claim 10 does not

depend from claim 1 which recites a definition of R and R' for formula II or from claim 9 which recites a definition of R'' for formula III, and does not incorporate limitations recited therein. The chemical formulas II and III do not in themselves recite what the groups R, R' or R'' mean. Therefore it is unclear what structures are encompassed by the formulas and what structures are excluded from the formulas because the R groups are undefined.

Claims 9, 15 and 22 recite "wherein R" is a protecting group, preferably acetyl or benzoyl". Claims 11, 14, 16-21 and 23-31 depend from claims 9, 15 and 22 and incorporate all limitations therein. This recitation renders the claims indefinite because it is unclear whether narrower limitation(s) following the phrase "preferably" are part of the claimed invention. See MPEP § 2173.05(d).

Claim 33 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite in that it fails to point out what is included or excluded by the claim language. This claim is an omnibus type claim. It is unclear what is "substantially" as described and what limitations "reference to steps 1 to 5 of the Example" requires.

Claim 37 recites the use of compound of formula II, III, IV, V in the synthesis of a compound of formula I. The recitations of formula II, III, IV, V and formula I renders the claim indefinite because the chemical formulas I-V do not in themselves recite what the groups R, R' or R'' mean. Therefore it is unclear what structures are encompassed by the formulas and what structures are excluded from the formulas because the R groups are undefined.

Claim 32 references "scheme 1", and therefore is not in itself complete. MPEP 2173.05(s) provides that where possible, claims are to be complete in themselves, and incorporation by reference to a specific figure or table is a necessity doctrine, not for applicant's convenience. Further, it unclear if the steps require the percent yield recited in scheme 1 at page 14 of the specification and whether a step using the specified reagents but giving a different percent yield is the same step. Therefore the incorporation by reference of scheme 1 renders the claim indefinite.

Claim Rejections - 35 USC § 112 and 101

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 37 provides for the use of a compound of formula II, III, IV V in the synthesis of a compound of formula I, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim 37 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under

35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Allowable Subject Matter

Claim 32 would be allowable if rewritten or amended to overcome the rejection under 35 U.S.C. 112, 2nd paragraph, set forth in this Office action.

The following is a statement of reasons for the indication of allowable subject matter:

The closest prior art is Schaeffer et al. (JACS, 1958, 82, p3738-3742, provided by Applicant in IDS mailed 6 Nov 2006) and Deghati et al. (Tetrahedron Letters, 2001, 41, p1291-1295, provided by Applicant in IDS mailed 6 Nov 2006).

Schaeffer et al. teaches nucleophilic aromatic substitution (page 3738, left column paragraph 2) of a dichloropurine with methanolic ammonia to displace a chloride (page 3739, chart I at top of left column and right column, paragraph 4). Schaeffer et al. teaches conversion of the 6-amino-2-chloropurine to 6-amino-2-methoxypurine (page 3740, left column, chart III and paragraph 2).

Schaeffer et al. does not specifically teach the method comprising the steps shown in scheme 1 (instant claim 32).

Deghati et al. teaches a method of synthesizing purine nucleosides via 2-nitroadenosine and 2-nitroinosine (abstract). Deghati et al. teaches synthesis of 6-chloro-2-nitropurine (page 1293, scheme 2). Deghati et al. teaches conversion of 6-

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chloro-2-nitropurine to 6-amino-2-nitropurine, then 6-amino-2-methoxypurine or spongosine (page 1294, scheme 3).

It would not have been obvious to one of ordinary skill in the art at the time of the invention to combine Schaeffer et al. and Deghati et al. to give the instant invention. Schaeffer et al. and Deghati et al. in view of the level of ordinary skill in the art at the time of the invention suggest methoxy, nitro and chloro are known to one of ordinary skill art as leaving groups for nucleophilic aromatic substitution. However, MPEP 2144.04 VI.C. provides "The mere fact that a worker in the art could rearrange the parts of the reference device to meet the terms of the claims on appeal is not by itself sufficient to support a finding of obviousness. The prior art must provide a motivation or reason for the worker in the art, without the benefit of appellant's specification, to make the necessary changes in the reference device." citing *Ex parte Chicago Rawhide Mfg. Co.*, 223 USPQ 351, 353 (Bd. Pat. App. & Inter. 1984). Schaeffer et al. and Deghati et al. and the level of ordinary skill in the art do not provide a motivation or reason to rearrange parts in the prior art method so as to make a 2,6-dimethoxypurine and then react the 2,6-dimethoxypurine to give 6-amino-2-methoxypurine. Therefore the instant invention is not taught or fairly suggested by the prior art because one of ordinary skill in the art would not have been motivated to combine the teaching.

Conclusion

Claims 1-31, 33 and 37 are rejected.

Claim 32 is rejected under 35 U.S.C. 112, 2nd paragraph.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jonathan S. Lau whose telephone number is 571-270-3531. The examiner can normally be reached on Monday - Thursday, 9 am - 4 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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